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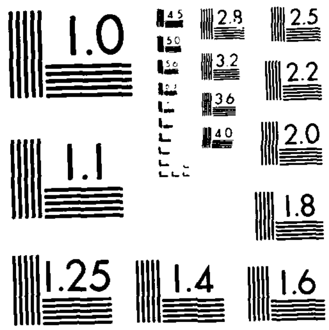
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VANDERBILT

*Progress Report on the*

**VANDERBILT FREE ELECTRON LASER PROJECT IN BIOMEDICAL AND MATERIALS RESEARCH**



for the period 1 February 1987 - 31 January 1988

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This report describes the research activities carried out during the first year of Vanderbilt's contract to develop a Regional Free Electron Laser Center under the auspices of the Medical FEL Program. A brief introduction to the scientific theme of the program is followed by reports on procurement actions to acquire an rf-linac-driven infrared free-electron laser and on the construction of the Vanderbilt Free-Electron Laser laboratory facility. A summary of research work in progress in six pre-FEL and FEL projects in clinical, biophysical and materials science applications follows, including studies of: thermal and nonthermal effects in wound healing; neurosurgical applications of lasers coupled to stereotactic imaging; biomembrane dynamics and drug action; FEL based studies of DNA dynamics; photon-matter interactions in crystalline and glassy materials typical of FEL resonator optics and beam-delivery systems; and designs for a radiological imaging experiment using Compton backscattered FEL photons. A summary of the FEL Review Panel meeting held in October 1987 at Vanderbilt is appended as the final section of the Report.

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*Progress Report on the*

# VANDERBILT FREE ELECTRON LASER PROJECT IN BIOMEDICAL AND MATERIALS RESEARCH

for the period 1 February 1987 - 31 January 1988

Supported by the Office of Naval Research and
the Office of Technology Applications, Strategic Defense Initiative Organization

Contract Number N00014-87-C-0146

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## I. Introduction

In 1987, the Office of Naval Research, acting as manager for the Congressionally-mandated Medical Free-Electron Laser Program, awarded a contract to Vanderbilt University to develop, construct and operate a free-electron laser facility dedicated to biomedical and materials studies, with particular emphases on

- fundamental studies of absorption and localization of electromagnetic energy on and near material surfaces, especially through electronic and other selective, non-statistical processes;
- non-thermal photon-materials interactions (*e.g.*, electronic bond-breaking or vibrational energy transfer) in physical and biological materials as well as in long-wavelength biopolymer dynamics;
- development of FEL-based methods to study drug action and to characterize biomolecular properties and metabolic processes in biomembranes;
- clinical applications in otolaryngology, neurosurgery, opthalmology and radiology stressing the use of the laser for selective laser-tissue, laser-cellular and laser-molecule interactions in both therapeutic and diagnostic modalities.

This program emphasizes selective enhancement, inhibition or disruption of biological, chemical and physical processes in the atomic, molecular, macromolecular, cellular and tissue regimes to modify the structure and function of organic and inorganic materials. The concern for electronic, as opposed to thermal, effects arises on the biomedical side from concern for minimizing undesirable collateral effects to surrounding tissue, whereas on the materials side it stems from the need to selectively make and break bonds or excite specific physical and chemical interactions.

The underlying scientific *leitmotiv* of the Vanderbilt program is the role of electronic processes in the photon-materials interaction, including the absorption, localization, transformation and dissipation of the incident photon energy. The overarching experimental paradigm is to track all the channels through which incident energy can flow as it is dissipated from the original local absorption site. This approach can be applied all across the spectrum of possible incident photon energies, and because it emphasizes *microscopic* (that is, atomic scale) dynamical features of the energy flow, allows a coherent attack across a broad front of problems in medicine (low-level radiation hazards and selective cytological photodisruption, for instance); molecular biology (the role of molecular vibrations in bioenergetics); materials science (infrared and far-infrared interactions and short-pulse radiation damage); and fundamental surface physics (time-resolved studies of energy flows in insulating materials).

Thus the Vanderbilt program brings together physicists, biomedical scientists and clinicians around a common FEL facility, but they use a common scientific paradigm to investigate problems as diverse as wound-healing in otolaryngological surgery, protein dynamics in lipid bilayers, and picosecond infrared laser photon interactions with glassy materials.

## II. FEL Procurement Action

Although the nominal starting date for the Vanderbilt FEL Project was February 1, 1987, contract negotiations were sufficiently protracted that "the check," duly back-dated, actually arrived in early July, 1987. At this point, the FEL Procurement Committee began to discuss the acquisition of an infrared free-electron laser suitable for biomedical and materials research.

In accordance with the original Vanderbilt proposal, we began discussions almost immediately with Sierra Laser Systems (SLS), the commercial licensee for the technology developed by Prof. John Madey for the Stanford Mark III ir-FEL. Ray Girouard, the Chief Executive Officer of SLS, visited Vanderbilt to discuss their proposal for construction of an FEL. At the first meeting, it was learned that the development of a "turnkey" FEL of the type originally proposed by Sierra was still some ways off in the development cycle, and we began to explore ways of acquiring something closer to the Mark III ir-FEL in order to come on-

line at a date more nearly consistent with the contract goals.

The technical design goals are now agreed upon, and will result in delivery of an ir-FEL to Vanderbilt with micropulse and macropulse specifications essentially identical to those of the current Stanford Mark III machine, but with a macropulse repetition frequency of 60 Hz to produce an average power in excess of 6 W. The engineering improvements required are believed to be straightforward extensions of recent significant improvements in the design of the Mark III electron gun, which has already shown more than a thirty-fold improvement in optical output power and energy during the past twelve months.

At the present time, contract negotiations are virtually complete with SLS, and the Vanderbilt administration are in the final phases of discussing our plans with government officials, including the Technology Applications Office of the SDIO which manages the Medical Free Electron Laser Program, to be certain that our plans are consistent with the overall program goal to develop a regional users facility and FEL Center of Excellence at the earliest possible date.

## III. FEL Laboratory Building

J. Anthony Fort
*Office of Campus Planning*

Ground was broken in July 1987 for the construction of a new Free-Electron Laser Laboratory to house the Sierra Laser Systems FEL and provide appropriate laboratory space in close proximity to Vanderbilt participants in the FEL Project.

After interviewing a number of architects for the design phase, the Project Leaders voted to award the design contract to the Seattle Office of the Austen Co., who have built, among many other major scientific projects, the Boeing FEL laboratory in Seattle. The design sequence was "fast-tracked," with the idea that either a "design-build" or a "design-construction management" approach could be considered during the initial building design phase.

Following completion of the building design, and interviews with a number of potential builders, Centex-Rodgers Construction Co. was selected as construction manager, with John Albert as Project Manager and Carroll Gordon as Construction Superintendent. With many years of experience in Nashville and elsewhere, the Centex-Rodgers team has produced outstanding results on a very short time scale. Excavation, drilling and blasting for the FEL Laboratory foundations began in late July, 1987. Substantial completion is anticipated in August, 1988.

Programmatic adjacency requirements played a major role in site selection. The facility is located in close proximity to (1) the Physics, Chemistry and Molecular Biology Departments of the College of Arts and Science; (2) the research facilities of the School of Medicine; and (3) the School of Engineering. Once the site was selected, physical site constraints became key ingredients of the building's form. Immediate programmatic needs could be served easily within the confines of the site; however, in order to allow the flexibility of future expansion, any increase in the building area had to be accommodated vertically. Moreover, the scale of surrounding buildings suggested that the building height should be restricted to two stories above grade. The immediately programmatic requirements for the facility could best be served below grade: there is a need for considerable radiation shielding for the FEL itself, and natural light has to be excluded from the user laboratory space if possible.

Within this context, Jack Smith, the architect and project manager for the Austin Co., designed the initial construction entirely below grade. When complete, present construction will provide two stories below a plaza at grade level, with mechanical equipment occupying enclosed space at one corner of the plaza. Access to the below-grade facility is provided by stair towers at either end of the plaza, and an elevator and loading dock adjoin the stair closest to an adjacent street. The building structure is designed to accommodate two additional future stories directly over the existing facility. The stair towers and elevator shaft are also designed for vertical expansion.

During excavation, the Users Committee requested that the lowest level, which provides the vault for the free electron laser and the associated power supplies, be expanded in size. Since the

lowest level was excavated from bedrock, the cost of space at this level was at a premium. Initial plans had provided a space 10 feet wide by 100 feet long for the FEL; the Sierra Mark III style FEL required a space only half this length; therefore, future expansion had been envisioned linearly. The Users Committee, however, foresaw that future requirements might mandate a recirculating geometry, in which case the extra length provided would be of little value. Accordingly, half the linear extent of the FEL vault space was widened to 19 feet. In addition, an X-ray beam transport tube was installed to allow for Compton back-scatter experiments by the Department of Radiology, and a beam line was laid to the nearby Engineering Building to permit the FEL photons to be employed in turbulent combustion studies using a supersonic wind tunnel apparatus to be made available in that structure.

Excavation, framing and concrete placement is now complete. As this report is written, roofing, masonry work on the exterior, and interior partition work is underway. Total gross area will be approximately 13,300 square feet. Excluding vertical circulation, the building footprint is approximately 100 feet by 70 feet. The lowest level will be devoted entirely to housing the FEL and its associated equipment. The level immediately above will house all of the multidisciplinary laboratory functions.

Two independent methods of beam delivery can be accommodated by the existing construction. The beam delivery paths, like the structure, may also be extended vertically. A joint study of the building vibration modes is being undertaken with members of the Federal Systems Division of the Kodak Corporation, who have significant expertise in beam delivery optical systems. The results of this study are expected to provide important guidance in the proper placement and structure for the mounts and beam-steering components of the delivery system, particularly for demanding applications such as laser microsurgery.

## IV. FEL/Pre-FEL Research Projects

The Vanderbilt FEL Project as originally funded by the Office of Naval Research incorporated five of ten proposed research projects designed to demonstrate the capabilities of the FEL as a major new research tool in clinical, biophysical and materials research.

- The effects of laser wavelength, pulselength and intensity on wound-healing following surgery on the airway.
- Neurosurgical applications of the FEL, including the use of stereotactic imaging systems to control the laser.
- The effects of pulsed laser irradiation on metabolic cycles at membranes, on crosslinking in large biomolecules and on drug action;
- Fundamental studies of laser interactions with DNA and of the link between molecular, cellular and tissue effects; and
- Studies of laser interactions at high intensities with crystalline and glassy materials typical of FEL optics and laser beam-delivery systems.

These five "demonstration" research projects were to be conducted partly with table-top laser systems, and, where appropriate, with other FEL facilities during the time when the Vanderbilt FEL was under construction.

### Thermal and Nonthermal Laser Effects in Wound Healing

Robert H. Ossoff, M.D.
James Duncavage, M.D.
David Zealear, Ph.D.
*Department of Otolaryngology*

The biomedical arm of the FEL project is currently at the end of a productive first year. Construction of the laser laboratories was completed and research was initiated with several collabo-

rating departments from both the Medical Center and the College of Arts and Science.

Models were established for studying the effects of laser radiation on cells in culture. In a series of studies, levels of $CO_2$ laser radiation were found to cause clumping of nucleic acid, which represents an intermediate level of cellular destruction. This was in contrast to the complete skeletonization of cells irradiated with higher, more injurious levels of radiation. In the same series of experiments, threshold levels of injurious laser radiation were determined for a number of cell types. These experiments are the basis for future research that can lead to laser modulation of biological function.

The initial step in any acute inflammatory reaction is the adhesion of neutrophils, cells that are in the blood stream, to the endothelium, cells that line small and large blood vessels. An experiment was conducted to determine the effects of $CO_2$ laser radiation on this adhesion. The results suggest that $CO_2$ laser radiation may have little or no effect on adhesion and thus may have a less prominent associated inflammatory response.

Studies were conducted to delineate the effects of continuous versus superpulsed infrared radiation on tissues. A commonly utilized $CO_2$ laser with its specific set of pulse parameters was used. It is interesting that the results were not consistent with what is traditionally accepted about superpulsed laser effects. Superpulse radiation caused shallower, but wider, temperature profiles compared to continuous radiation. These experiments suggest that tissue effects are not only related to pulsing or non-pulsing of laser radiation, but also to the parameters of pulsing. This study is the first of many that will help determine appropriate pulse paradigms for specific tissue effects.

As an initial step in determining the potential for laser nerve welding, experiments were conducted to determine at what energy levels will a nerve be damaged by a laser, but still conduct impulses. These energy levels are the upper limits of what can be used to weld vessels. In upcoming experiments nerves will be welded using this information and the mechanism of welding, physical properties of the weld, and the regeneration potential of welded nerves will be investigated.

*E. Coli* bacteria were irradiated with varying energies of 532 nm laser light to determine a dose response curve. An $LD_{50}$ and $LD_{100}$ were determined. Spectral analysis of the bacteria was consistent with a high absorption peak at 532 nanometers. The mechanism of bacterial destruction is unclear, but there is a hint that it may be non-thermal. This study is one of a series investigating the potential for lasers in sterilizing both tissues and surgical equipment.

FEL Project-Supported Personnel

M. Nair, cell culture technician
N. Houchin, laser technician

## Neurosurgical Applications of the FEL

Robert Maciunas, M.D.
*Department of Neurosurgery*

During this past year, Mr. V. Mandava, our image processing research associate, and I have developed a common image-reading platform program for accessing data tapes from digital image modalities, such as the CT, MR, DSA, SPECT, gamma camera, and video digitized input from analog radiographs, for detecting brain tumor margins. Preliminary development of a segmentation program for edge definition and manipulation of the defined volume has begun; this is to interface with servo-driven laser resection methods for stereotactic laser craniotomies. The next objective is rotating and manipulating the tumor target volume in three-dimensional space prior to imaging-driven laser resection.

Ms. Lisa Hardin, a research laboratory technician, and I have begun the cataloging of temporal and spatial thermal profiles of various laser wavelengths using currently available research lasers, such as $CO_2$, KTP532 (a frequency-doubled, Q-switched Nd:YAG laser), and excimer, on cerebral tissue. Thermocouples linked to a rapid-sampling A/D converter plot the thermal data, and histologic sections of lased tissue provide morphological correlation. Clinical correlations for observed thermal dispersion curves have been documented during the year in laser craniotomies. Nonthermal or sub-thermal effects directly affecting cellular viability and proliferation for a similar spectrum of laser irradiation are being

studied in a cerebral glioma tissue culture model. Dose-related nonthermal cellular injury has been identified. Further studies to characterize thermal and nonthermal effects of different wavelengths of laser irradiation are scheduled for the next year.

FEL Project-Supported Personnel

Lisa Hardin, cell culture technician

## Structure and Function of Membrances

Sidney Fleischer, Ph.D.
J. Oliver McIntyre, Ph.D.
Becca Fleischer, Ph.D.
*Department of Molecular Biology*

We had originally proposed three different kinds of projects using the FEL to study structure and function of biomembranes. We have initiated studies for projects I and III, the results of which are summarized in the following.

Project I *Dynamic Characteristics of Biomembranes and Membrane Proteins*

The goal of this project is to apply the FEL as an excitation source for fluorescence and absorption anisotropy spectroscopic studies to characterize the motion of membrane proteins and to relate such motion to catalysis. Pre-FEL studies have been carried out with 3-hydroxybutyrate dehydrogenase (BDH) which requires phosphatidylcholine (PC) for catalysis and is one of the best-studied lipid-requiring membrane enzymes. We have begun studies to characterize the dynamic properties of BDH reconstituted into phospholipid vesicles both in the presence and absence of PC by fluorescence lifetime and time-dependent anisotropy. Studies were carried out using the fluorometry facilities at the University of Illinois at Urbana together with our collaborator, Enrico Gratton. Multifrequency phase and modulation fluorometry, with excitation from a sync-pumped, mode-locked, cavity-dumped dye laser system, was used to obtain fluorescence lifetime and time-dependent anisotropy data for both the intrinsic fluorescence (tryptophan) of BDH as well as for BDH covalently derivatized with IAEDANS. Lifetime data were analyzed independently (two or three component analyses) as well as with a model-dependent global analysis. The data indicate that the tryptophan fluorescence of BDH exhibits three lifetime components which are similar in the presence versus absence of PC, suggesting that the environment and motional charactristics of the tryptophan of BDH are not modulated by PC. For the IAEDANS-BDH, three lifetime components were also detected, the largest of which was 17.2 nsec 20°C and 18.9 nsec at 0°C. With this probe, time-dependent anisotropy data yielded rotational correlation times of $2.2 \times 10^{-7}$ sec and $4.7 \times 10^{-9}$ sec for the spectral component with 17.2 nsec lifetime.

Preliminary studies were carried out with the calcium pump protein, a transmembrane ion pump. The pump protein was labeled at unique sites with either IAEDANS or FITC or EOSIN. Preliminary characterization of these samples was carried out using a steady state fluorescence instrument which showed that lifetime and time-dependent anisotropy studies are feasible. We have recently received part of our multi-frequency phase and modulation fluorometer and now anticipate rapid progress with the studies outlined in our proposal.

Project III *Explore Development of a General Crosslinking Technology With Application to Drug Action*

The overall aim of this work is to explore whether the FEL can be used to induce selective and specific crosslinking with components in a biological membrane. Two model membrane systems available in our laboratory have been used to investigate crosslinking: (i) the calcium release channel of skeletal muscle terminal cisternae of sarcoplasmic reticulum; and (ii) the UMP transporter in the Golgi apparatus.

(i) The $Ca^{2+}$ release channel of the terminal cisternae of sarcoplasmic reticulum (SR) is involved in $Ca^{2+}$ release, thereby triggering muscle contraction. The channel is specifically blocked by the drug, ryanodine. The purified channel has been isolated in our laboratory and has been identified as a high molecular weight polypeptide (Mr ~ 360 KD). Therefore, we know which polypeptide should get labelled when the crosslinking is selective. A purified preparation of terminal cisternae of SR containing ryanodine receptor (15 pmoles/mg protein) was incubated with 3 $\mu$M [$^{3}$H]-ryanodine (absorption maximum 267 nm) in the presence of either 25 $\mu$M $Ca^{2+}$ or 2.5 mM EGTA. Aliquots were frozen and exposed to a

308 nm light beam from a Xenon chloride excimer laser (350 mjoules pulse$^{-1}$, 60 pulses sec$^{-1}$) for varying times up to 10 sec, or to 267 nm light from a 150 W Xenon arc lamp for up to 30 min. Preliminary results showed measurable covalent binding of the $^3$H-ryanodine (~0.01 pmoles/mg protein) induced by the 267 nm light but little or no covalent binding by illumination with the 308 nm laser (exciting at the edge of the ryanodine absorption). In both cases, the polypeptide profile, characterized by one-dimensional polyacrylamide gel electrophoresis in sodium dodecyl sulfate (SDS-PAGE), was similar before and after illumination indicating the absence of polypeptide crosslinking under these conditions. We are planning to follow up these experiments using illumination from a dye-laser with the frequency tuned closer to the region of the absorption maximum of the ryanodine ligand.

(ii) The Golgi apparatus functions as an intermediary in the transport and processing of proteins and lipids from the endoplasmic reticulum to their final destination, both extracellular (secreted products) and intracellular (plasma membrane and lysosomes). A variety of enzymic modifications of the transported protein and lipids occur in the Golgi apparatus; the transport of substrates and products across the Golgi membrane are fundamental to these modification processes. Products of glycosylation and sulfation in the Golgi lumen include nucleoside monophosphates such as UMP and AMP. Studies in our laboratory have demonstrated the presence of a UMP transporter that is specific for pyrimidine monophosphates and has saturable binding with a $K_b$ of ~20 µM at 37$^0$C. We have initiated studies to identify the UMP transporter in Golgi using the crosslinking approach. Purified Golgi from rat liver were incubated with 5 µM $^{14}$C-UMP and, after freezing, were illuminated with 256 nm light for varying periods of times. We found that $^{14}$C label from $^{14}$C-UMP (up to 9.6 pmoles per mg protein) was covalently incorporated into the Golgi membrane and incorporation was quantitatively inhibited by excess unlabeled UMP. This photolysis procedure also resulted in selective crosslinking of specific membrane proteins as revealed by one-dimensional SDS-PAGE which showed a time-dependent increase in high molecular weight protein bands concomitant with a decrease in staining intensity of a number of specific polypeptides separated by the gel.

The results from both these studies suggest that selective photochemical crosslinking of both ligands to their receptors (to identify specific receptors) and polypeptides with each other (to identify specific protein-protein association in membranes) by utilizing a high intensity tunable photon source, such as an FEL, are feasible. We are planning to continue pre-FEL studies with these two systems using high intensity laser illumination of the samples at a number of frequencies and then to extend the studies to other ligand-receptor and protein-protein interactions as outlined in our proposal.

FEL Project-Supported Personnel

Becca Fleischer, Research Associate Professor
J. Oliver McIntyre, Research Assistant Professor
Sidney Fleischer, Professor

## Mechanisms of Laser-Tissue Interaction and Clinical Applications

Glenn Edwards, Ph.D.
John Kozub
Changle Liu
*Department of Physics and Astronomy*

Robert Ossoff, M.D.
Al Aly, M.D.
*Department of Otolaryngology*

As stated in the original proposal "the theme of this project is the targeting of electromagnetic energy into diseased tissue, with an emphasis on selective laser-tissue interactions matched to cellular characteristics that are unique to the diseased tissue. In order to establish selective methods of interaction, the first goal of the project is to characterize the frequency specific mechanisms of absorption by DNA, proteins and lipids as a function of intensity and pulse duration. The second goal is to determine the lifetimes of the various excited states; this information will suggest parameters for ultrafast pulses that will maximize the nonthermal relative to the thermal effect. The third goal of this project is to refine these pulse parameters to optimize selective tissue interaction and thus produce the desired clinical effect."

During the past year we have undertaken a number of steps to initiate this research effort: the

steps include assembling qualified personnel, developing a number of spectroscopic systems for pre-FEL and dual-beam FEL experiments, initiating pre-FEL experiments at Vanderbilt, and performing experiments at existing FEL centers. Progress for each of these steps will be addressed below.

*Personnel.* This research effort calls for interdisciplinary expertise and cooperation. Towards this end we have added a number of collaborators to the original investigators. Two graduate students in the Department of Physics and Astronomy are supported as research assistants by the contract and are working with Professor Edwards on problems that will evolve into their dissertation topics. Both of these students came to Vanderbilt to work in this research area. John Kozub has just finished his first year and is investigating the manner in which electromagnetic radiation interrupts the natural interaction of biopolymer systems. It is worthwhile to point out that John has been quite successful during his first year and has recently been nominated by the Graduate Program Committee to receive Vanderbilt's Lagemann Award presented to "the most promising entering or first-year graduate student in the Department of Physics and Astronomy." The other student is Changle Liu, an advanced graduate student. who left Purdue University to take advantage of Vanderbilt's graduate program in experimental biophysics. Changle joined the department only four months ago and is investigating the effect of pulsed radiation on biopolymer systems. In addition to these physics graduate students, Al Aly, M.D., a medical research fellow associated with Dr. Ossoff, is working in close collaboration with the physicists in developing the irradiation protocols for laser-tissue interaction studies.

*Equipment.* During the past year we have exerted a significant effort to develop two different spectroscopic systems. One of these systems is the Hewlett Packard 8510 Network Analyzer. We have modified this spectrometer to allow an alternative calibration scheme that greatly enhances reproducibility and yields high precision measurements of biological solutions and tissue. This project required significant software/hardware development. For the past three months we have been measuring biopolymer solutions and cellular suspensions with good preliminary results. The second radiation source is a Quantel Nd:YAG pumped dye laser system that is to be used as a nanosecond or picosecond lasr for both pre-FEL and dual-beam FEL experiments. Currently this laser is being integrated into a complete spectroscopic system for biophysical research. The laser arrived only a month ago and is currently operating at specification and is being modified for lasing in an extended wavelength regime.

In order to produce and characterize biopolymer samples we have developed a nearly complete laboratory of molecular biology in the first floor of the Department of Physics and Astronomy. Since early this spring we have been producing large quantities of purified DNA samples for spectroscopic investigation.

*Pre-FEL Experiments.* As mentioned above, we have performed a number of preliminary experiments investigating the fundamental mechanisms of laser-tissue interaction. We have measured the infrared absorption properties of DNA which is an essential step in the series of experiments that will determine the lifetime of the various excitations. In addition, we have measured the ultraviolet scattering and absorption properties of cell suspensions with intriguing results in laser induced cell death. During the summer we will extend these measurements beyond the preliminary stages.

During the summer we will begin a series of experiments investigating the effect of pulsed radiation of DNA protein interactions. In particular, we will monitor the effect of radiation induced changes on the cell and related clinical applications.

*FEL Experiments.* During the past year we have been planning a series of experiments for the far-infrared FEL at the University of California, Santa Barbara. The pulsed nature of the UCSB FEL, as enhanced by switching techniques, will be used to measure the homogenous and inhomogeneous nature of the broadening of DNA features in the infrared. This will allow us to determine the lifetime of these modes. Although a minimum lifetime has been determined by cw experiments, a more accurate estimate of the lifetime is necessary in order to design an exposure protocol that will optimize the resonant effect.

## Photon-Matter Interactions in Model Optical Materials for FEL Beam Delivery Systems

Richard F. Haglund, Jr.
Norman H. Tolk
*Department of Physics and Astronomy*

Donald L. Kinser
Robert A. Weeks
*Department of Materials Engineering*

(NB: During 1987, this work was supported through Contract N00014-K-0735, an Office of Naval Research pre-FEL research contract in the FEL Materials program.)

Rf-linac driven free-electron lasers, with their unique combination of high macropulse and micropulse peak power, high pulse repetition frequency, and trains of ultrashort pulses, deliver photons in uniquely insulting ways to the components of the associated optical systems. For the technology of free-electron lasers, the damage caused by these pulses in the FEL resonator optics is a practical problem of utmost concern, since it is the limiting factor in the optical output of the device and often imposes severe constraints on resonator optimization. In the medical environment, this characteristic of the FEL will challenge the present understanding of laser-induced damage in materials, whether we are talking about questions of optical fiber performance in surgical delivery systems, or inadvertent laser interactions with other apparatus (e.g., endotrachael tubes, bronchoscopes and similar tools) used to facilitate laser surgery and medicine. In both cases, the materials physics of the FEL photon-matter interaction poses questions of great scientific interest and enormous, direct technological relevance.

Studies on the ways in which the electronic energy of photons is absorbed, localized, transformed and ultimately dissipated are showing that there are many pathways leading to surface and bulk damage to typical optical materials, such as alkali halides, alkaline earth halides, metal oxides and fused silicas. This is particularly true if the photons are delivered, as is the case with the FEL, on time scales comparable to or shorter than the thermal relaxation times.

Virtually of the previous work on the interactions of laser photons with matter has focused on thermal models for the observed effects, because they were, in principle, easy to conceptualize and calculate. But rate constants for processes like optical damage have proven difficult or impossible to calculate because the initial rate-limiting steps are unknown. Indeed, in the picosecond laser regime, it is quite likely that the thermal model must be entirely abandoned because the preconditions for its validity -- namely, the establishment of a local thermodynamic equilibrium -- do not obtain. Electronic processes occur on the time scale of a single vibrational period and under many circumstances are incapable of exciting anything more collective than a single molecular vibration. These concerns underly the critical importance of using bright, tunable, ultrashort probes -- of which the FEL appears to be the most promising -- to study electronic and other nonthermal excitation processes in organic and inorganic materials.

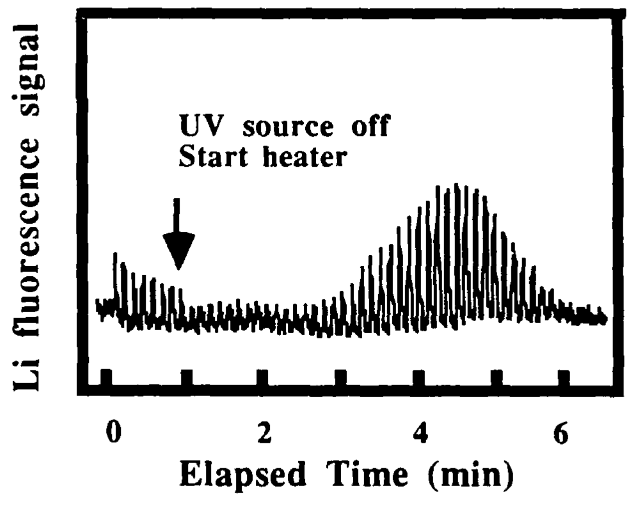
During the year, we have studied photon-induced damage to model wide band-gap optical materials, such as alkali halides, alkaline earth halides and fused silicas. We have been focusing particularly on modifications to surface composition, surface electronic structure, and loss of surface and near-surface atoms due to atomic and molecular desorption. These studies have included both laser-induced desorption and ultraviolet-photon-stimulated desorption using the newly developed Vanderbilt-SRC partnership beam line at the Aladdin Synchrotron Radiation Center at the University of Wisconsin, Madison.

We have found that even minute changes in surface chemical composition -- whether due to the metallization of the surface stemming from the energetic photon-induced expulsion of the nonmetallic component of a dielectric, or due to the adsorption of small quantities of gases -- can inhibit or entirely close certain desorption channels. In addition, time-resolved studies have provided new insight into the role played by the energetic decay of the self-trapped exciton (STE) as the precursor to desorption events. The STE may be viewed as a phase transition of a photon-created electron-hole pair in which the relevant scale parameter is the effective mass of the hole; the temporary localization of the incident photon energy is made possible by this phase transition in an ordinary Frenkel exciton. The lattice deformation

caused by the STE, in turn, provides the kinetic energy needed to expel an atom or atoms from the surface of the material, producing damage on an atomic scale to the host lattice.

These desorption-induced changes in the surface not only change the thermal properties of the surface, but also its electronic properties. These effects occur for photon energies below the bulk band-gap energy; hence, the surface metallization following desorption of ground-state non-metallic atoms is expected to be important in pulsed laser irradiation of surfaces, and may even, in the case of ultraviolet lasers, occur via single-photon transitions.

We illustrate this effect with data from a recent experiment on photon-stimulated desorption of LiF, showing the development of a layer of metallic Li on the surface of a pure LiF crystal irradiated by ultraviolet photons in an ultrahigh vacuum environment. The radiation source was the first-order light from the Aladdin synchrotron light source of the University of Wisconsin.




*Fluorescence signal from Li$^o$ desorbed by the "white" ultraviolet photon spectrum from the Aladdin synchrotron light source. At the beginning of the measurement, the LiF crystal is illuminated for about a minute by the uv photons; then the uv irradiation is blocked by a beam stop, and the crystal is heated, while the laser-induced fluorescence signal from desorbing Li$^o$ is monitored.*

The Figure shows the time evolution of the first resonance decay of the desorbed Li$^o$ excited by light from a tunable dye laser. Each peak in this spectrum represents a scan of the Coherent 599-21 tunable dye laser lasting approximately ten seconds over the first resonance line of the Li atoms at 6707 Å. At the time indicated by the arrow, the synchrotron light was blocked, and the LiF crystal was heated ballistically by turning on the heater block of the sample holder. As the sample temperature increases, the yield of Li$^o$ increases at first, as metallic Li is desorbed thermally from the surface. As this surface layer of neutral Li is depleted, the laser-induced fluorescence signal gradually dies away. The fact that it does not decay completely is consistent with the long time scales for F-center diffusion seen in previous experiments.

During the past year, the first experiments using excimer-pumped dye laser to do wavelength and intensity dependent measurements of these kinds of photon-induced damage studies were begun; work will continue in the coming year on optical materials of direct interest to the FEL materials problem.

FEL-Project Supported Personnel

Shirley Roth, Graduate Research Assistant
Dwight P. Russell, Research Associate

## Radiological Imaging Studies Based on Compton Backscattering of FEL Photons from the FEL Electron Beam


Frank Carroll, M.D., F.C.C.P.
Ronald R. Price, Ph.D.
David R. Pickens, III, Ph.D.
William H. Stephens, M.S.
*Department of Radiology and Radological Sciences*


This project, though not funded at present by the MFEL Program contract, has developed during the past year to become a significant part of the FEL activities at Vanderbilt, and shows significant promise for future research.

Since the potential diagnostic utility of monochromatic x-rays is so great, a partnership has been

established between the Department of Radiology and Radiological Sciences and the Kodak Corporation to undertake feasibility studies, early electron-beam design and optical beam design for fabrication of a Compton back-scatter device which will produce tunable X-rays in the keV range for diagnostic imaging. A modest grant has already been provided by the Kodak Corporation for preliminary design work on the device. In addition, a collaborative effort has also been established with scientists at the Oak Ridge Electron Linear Accelerator facility.

The construction design of the Vanderbilt FEL facility has now been modified to include a twelve-inch beam line into Target Room 2 on the second floor of the FEL laboratory. This beam-line has been designed and completed as an extension of the FEL vault, and was paid for in its entirety through grant monies from the Department of Radiology and Radiological Sciences. During the coming year, electron beam design and design of the optical components for the interaction region where the Compton-backscattered photons are created will be a primary activity for the collaborating scientists.

Although Kodak has made a commitment to future grants on a year-to-year basis for this project, these will not be of the magnitude required to fabricate the entire Tunable X-ray Imaging facility. We are presently seeking additional funding for the completion of the project.

## V. Program Office Activities

The Vanderbilt FEL Project for Biomedical and Materials Research became something more than heaps of file folders in faculty offices in August 1987 with the arrival of Ms. Pat Myatt as Project Secretary. The Project Office has coordinated a number of important activities in addition to the day-to-day management chores associated with mailings, budgeting and scheduling. These included the convening of the FEL Review Panel, setting up a system for ordering and tracking major items of supporting equipment for the Project, and helping to organize the standing committees that, for now, are helping to develop the Users Group at Vanderbilt.

### FEL Review Panel

In 1986, Vanderbilt proposed to the Office of Naval Research an interdisciplinary research program based on the use of a free-electron laser, with special emphasis on non-thermal photon-matter interactions of interest in the biomedical and materials sciences. This theme was a logical outgrowth not only of the research interests of the collaborators in the ONR proposal, but also of FEL-related work on mechanisms of ultraviolet photon-stimulated desorption in optical materials already funded by the ONR in Vanderbilt's Center for Atomic and Molecular Physics at Surfaces. Our FEL proposal contemplated acquisition of a high-peak-power FEL in the 2-10 μm range as the first step of the research program, with phased development of additional capability in the visible, ultraviolet, and far-infrared regions of the spectrum at a later date. The University has committed significant support to a long-range program in FEL development and applications, including funding for a dedicated FEL laboratory building now under construction.

Because the FEL researchers from the School of Medicine needed a laser capable of surgical studies using animal models, and because of the general interest in the picosecond dynamics of selective bond-breaking mechanisms in both inorganic and biological materials, the FEL Project leaders concluded prior to the submission of our original proposal that a long-pulse machine (of the type constructed by Luis Elias at Santa Barbara) was inappropriate to our scientific program. However, as Vanderbilt FEL researchers have investigated the machine issues relevant to our research program, it has become clear that there is a spectrum of short-pulse FEL technologies presently reduced or reducible to practice; in turn, any given choice of FEL technologies has a significant impact on the scientific program which can be mounted using that FEL.

In light of the long-range commitments to the FEL program made by the University, the Vanderbilt FEL project leaders decided to convene a Review Panel in Nashville in October, 1987 to evaluate short-pulse FEL technology options, prior to initiating FEL procurement. The Panel was chaired by Andrew Sessler (Lawrence Berkeley Laboratory), and included Bruce Danly (MIT Plasma Fusion Center), Christoff Leemann

(Continuous Electron Beam Accelerator Facility), Brian Newnam (Los Alamos National Laboratory), and Samuel Penner (National Bureau of Standards). At the request of the FEL project leaders, Todd Smith and Alan Schwettman of Stanford University prepared a presentation for the Panel on the status of FELs based on superconducting electron accelerator technology; John Madey, also of Stanford, and a group representing Sierra Laser Systems, Inc. presented relevant perspectives on high-peak-power room-temperature FELs. CPT Charles Houston, Manager of Technology Applications of the Strategic Defense Initiative Organization, and Dr. Howard Schlossberg of the Physics Division of the Air Force Office of Scientific Research, attended as observers.

## Summary of the FEL Panel Report

The Panel's report outlined the ways in which various choices of FEL technology would affect both our scientific opportunities and the shape of Vanderbilt's FEL program. The conclusions of the Panel may be summarized as follows:

- The essential choice is between a high-peak-power FEL, such as the infrared FEL built by John Madey at Stanford ("Option A" in the Panel's report), and a high-average-power FEL, using either a super-conducting or a room temperature recirculating electron linac ("Option B").

- Option A gives the simplest machine configuration in the near term, and Professor Madey's design can be cloned using more or less standard subsystems. Recent experience at Stanford indicates that such a machine is robust, reliable, and can deliver FEL beams suitable for a variety of users.

- Option A will produce the high peak powers desired for biomedical laser studies, and has some flexibility for changing in wavelength and temporal pulse structure. If certain upgrades are carried out, this FEL can meet some of the near-term needs of biophysical and materials science as well.

- Option B provides maximum flexibility in temporal pulse structure and tunability, as well as high average power. However, incorporation of a high peak power option may not be easy, and that would make the "Option B" FEL less useful, at least initially, to the biomedical researchers.

- The construction of the "Option B" machine now would require significant design effort, take substantial additional time (compared to Option A), and probably cost one and a half or two times as much as Option A.

While the Panel felt that Option A was obviously in accord with the currently mandated program goals, it also noted that Option B would be far more attractive to the kind of top-flight scientist Vanderbilt hopes to attract as Director of the FEL program. Indeed, the Panel's advice highlights the way in which programmatic and scientific considerations are closely intertwined. There is also, of course, a danger in pursuing "Option B" to get the "ultimate machine": if it takes too long to design and construct the FEL, no matter how good it may be in the end, the users' community may find it more profitable to pursue research using conventional lasers.

The FEL Project leaders and the Executive Committee have carried on significant discussions and with the members of the Panel, other principals in the national and international FEL communities, and the project managers in the Strategic Defense Initiative Organization and the Office of Naval Research. We have concluded that Option A followed by a suitably phased approach to Option B is the best choice for Vanderbilt, both scientifically and programmatically. The reasons for this conclusion were summarized in a report which circulated to the sponsoring agencies and the members of the Panel. It is available upon request from the FEL Project Office.

FEL-Project Supported Personnel

Pat Myatt, Secretary/Administrative Assistant
Venka Mendava, computer scientist
Lin-Jun Wang, laser physicist

## VI. Presentations and Publications

Talks and publications based on research supported under the Medical Free Electron Laser Program are listed, more or less chronologically, below.

### Conference Talks and Other Presentations

Richard F. Haglund, Jr., "Electronic Transitions in Surface and Near-Surface Radiation Effects," invited talk at the Fourth International Conference on Radiation Effects in Insulators (REI-4), Lyons, France, July 6-10, 1987.

Glenn S. Edwards, "Vanderbilt University FEL Center for Biomedical and Materials Research," Ninth International Free Electron Laser Conference, Williamsburg, VA, September 13, 1987.

Robert H. Ossoff, M.D., "The Vanderbilt Free Electron Laser Center for Biomedical and Biomaterials Research," ICALLEO, San Diego, CA, November 8-12, 1987

Richard F. Haglund, Jr., "Damage to Intracavity Optics from Electrons, Ions and Ultraviolet Photons," invited talk at the Los Angeles meeting of the SPIE (OE-Lase '88), January 10, 1988.

Richard F. Haglund, Jr., "Scientific and Technological Applications of Ultraviolet Desorption Spectroscopy," OSA Workshop on VUV and XUV Free Electron Lasers, Cloudcroft, NM, March 4, 1988.

Al Aly, M.D., "Laser Tissue Interactions," SDIO Technology Transfer Panel Meeting. San Antonio, TX, March 17, 1988.

Richard F. Haglund, Jr., "Technology Transfer: Hardware, Software, Models," SDIO Technology Transfer Panel Meeting, San Antonio, TX, March 17, 1988.

John Laurenzo, "The Effects of $CO_2$ Laser Radiation on Fibroblasts in Culture," National Student Research Forum. Galveston, TX, April 6-9, 1988

Robert H. Ossoff, M.D., "Free Electron Lasers in Otolaryngological Research," Communicative Disorders Foundation, Caneel Bay, April 9-16, 1988

Richard F. Haglund, Jr., "Free-Electron Lasers: A New Kind of Photon Factory for Science and Medicine," Department of Electrical Engineering seminar, University of Kentucky, April 21, 1988.

"The Effects of $CO_2$ Laser Radiation on Endothelial Cells and Endothelial-Neutrophil Adhesion," Al Aly, M.D., ASLMS, Dallas, TX, April 26, 1988.

### Papers Submitted or Published

G. S. Edwards and N. H. Tolk, "The Vanderbilt University FEL Center for Biomedical and Materials Research," Proceedings of the Ninth International FEL Conference, Williamsburg 1987. Nuclear Instruments and Methods in Physics Research A, in press.

R. F. Haglund, Jr., N. H. Tolk, G. M. Loubriel and R. A. Rosenberg, "Thresholds and Time-Dependence of Electron- and Photon-Stimulated Desorption in Alkali Halides," Nuclear Instruments and Methods in Physics Research **B18** (1987) 487.

R. F. Haglund, Jr., M. H. Mendenhall, N. H. Tolk, G. Betz and W. Husinsky, "Electronic Transitions in Surface and Near-Surface Radiation Effects," Nuclear Instruments and Methods in Physics Research B, in press.

R. F. Haglund, Jr., "Damage to Intracavity Optics from Electrons, Ions and Ultraviolet Photons," Proceedings of the SPIE **890**, in press.

### Papers in Preparation

Al Aly, Richard Hoover, Caroline Kerr and Robert H. Ossoff, "The Effects of $CO_2$ Laser Radiation on Endothelial Cells and Endothelial-Neutrophil Adhesion," to be submitted to Lasers in Surgery and Medicine.

Nels Gunnerson, Kirk Lane, Al Aly, Glenn Edwards and Robert Ossoff, "The Effects of 532 Nanometer Laser Radiation on Bacteria," accepted for oral presentation by the Bulletin of the American College of Surgeons, also to be submitted for publication.

James Duncavage, Al Aly, Robert Ossoff, Daniel Tench and Glenn Edwards, "Superpulse Versus Continuous Mode $CO_2$ Laser Radiation Delivery," accepted for presentation at the International Congress of Laser Surgeons, also to be submitted for publication.

Robert Maciunas, Al Aly and Robert Ossoff, "The Dissipation of Thermal Energy Away from Laser Craters," to be submitted for publication.

Marjorie Korff, David Zealear, Mitchell Schwaber and Robert Ossoff, "An Investigation of the Potential for Laser Nerve Welding," accepted for presentation by the American Academy of Otolaryngology, also to be submitted for publication.

R. F. Haglund, Jr., A. V. Barnes, M. H. Mendenhall, and D. A. Ramaker, "Competition between Surface and Bulk Processes in Photon-Stimulated Desorption of Lithium from Lithium Fluoride," to be submitted to Physical Review B.

Richard F. Haglund, Jr. and Norman H. Tolk, "XUV-VUV Free Electron Lasers in Ultraviolet Desorption Spectroscopy," to be submitted to the special issue of the Journal of the Optical Society on "The Physics of Free Electron Laser Applications."

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